AF/1631

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re application of:			
Nordine CHEIKH *et al.*		Art Unit:	1631
Appln. No.:	09/300,482	Examiner:	M. A. MORAN
Filed:	April 28, 1999	Atty. Docket:	16517.216
For:	**Nucleic Acid Molecules and Other MoleculesAssociated with the Phosphogluconate Pathway**	Confirmation No.	4511

APPELLANT'S BRIEF

Mail Stop Appeal Brief – Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

This is an Appeal from the Final Rejection of all claims pending in the above-captioned patent application. A Notice of Appeal was filed on July 12, 2004. Authorization to charge the official fees for this filing is given in the accompanying transmittal letter.

1. Real Party in Interest

The real party in interest is Monsanto Company, a Delaware corporation with offices at 800 North Lindbergh Boulevard, St. Louis, Missouri 63167.

2. Related Appeals and Interferences

Appellant identifies the following judicial proceeding, which may have a bearing the Board's decision in the present Appeal. On May 27, 2004, the Real Party in Interest in the above-captioned matter filed an appeal to the United States Court of Appeals for

the Federal Circuit in from a decision by the Board in *In re Fisher.* (U.S. Appln No. 09/619,643, B.P.A.I. Appeal No. 2002-2046, Fed. Cir. Case No. 04-1465). The Federal Circuit's decision in *In re Fisher* may have a bearing on the Board's decision with regard to at least one of the grounds of rejection in the present appeal. A copy of the Board's decision in Appeal No. 2002-2046 is attached hereto as Appendix B.

3. Status of Claims

Claims 1, 2, 10-13, 15-22 and 24-31 are pending. Claims 3-9, 14 and 23 were cancelled without prejudice to or disclaimer of the subject matter claimed therein in amendments filed October 17, 2002, September 17, 2003 and February 2, 2004. Claims 1, 2, 10-13, 15-22 and 24-31 stand finally rejected under 35 U.S.C. §§ 101 and 112, first paragraph. Appellant appeals all of the rejections of claims 1, 2 10-13, 15-22 and 24-31.

4. Status of Amendments

Appellant has not filed any responses subsequent to Final Rejection in this case.

5. Summary of Claimed Subject Matter

The claimed subject matter is directed to a substantially purified nucleic acid molecule that encodes a maize or soybean phosphogluconate pathway enzyme or fragment thereof, where the maize or soybean phosphogluconate pathway enzyme is selected from the group consisting of: (a) glucose-6-phosphate-1-dehydrogenase; (b) D-ribulose-5-phosphate-3-epimerase; and (c) phosphoglucoisomerase; where the substantially purified nucleic acid molecule comprises a nucleic acid sequence that hybridizes under conditions of 6.0 X sodium chloride/sodium citrate (SSC) at about 45°C, followed by a wash of 2.0 X SSC at 50°C to a nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 1, 225, 619 and complements thereof. Specification at page 14, line 2 through page 15, line 17 and page 43, line 13 through page 45, line 4. The claimed subject matter is also directed to an

isolated nucleic acid molecule comprising a sequence that hybridizes under conditions of 6.0 X sodium chloride/sodium citrate (SSC) at about 45°C, followed by a wash of 2.0 X SSC at 50°C to a nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 1, 225, 619 and complements thereof. *Id.* The claimed subject matter is also directed to an isolated nucleic acid molecule, where the isolated nucleic acid molecule comprises a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 1, 4, 14, 27, 225, 298, 311, 356, 569, and 619 or complements thereof. Specification at page 45, lines 5-19. The claimed subject matter is also directed to a substantially purified nucleic acid molecule that encodes a maize or soybean 6-phosphogluconate dehydrogenase or fragment thereof, comprising a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 14, 27 and complements thereof. Specification at page 20, lines 17-22. The claimed subject matter is also directed to a substantially purified nucleic acid molecule that encodes a maize or soybean phosphogluconate pathway enzyme or fragment thereof, where the maize or soybean phosphogluconate pathway enzyme is selected from the group consisting of: (a) glucose-6-phosphate-1-dehydrogenase; (b) D-ribulose-5-phosphate-3-epimerase; (c) ribose-5-phosphate isomerase; and (d) transaldolase; where the substantially purified nucleic acid molecule comprises a nucleic acid sequence that hybridizes under conditions of 6.0 X sodium chloride/sodium citrate (SSC) at about 45°C, followed by a wash of 0.2 X SSC at 50°C to a nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 4, 298, 311, 569 and complements thereof. Specification at page 14, line 2 through page 15, line 17 and page 43, line 13 through page 45, line 4. The claimed subject matter is also directed to an isolated nucleic acid molecule comprising a sequence that hybridizes under conditions of 6.0 X sodium chloride/sodium citrate (SSC) at about 45°C, followed by a wash of 0.2 X SSC at 50°C to a nucleic acid molecule comprising a nucleic acid sequence selected from the group

consisting of SEQ ID NOs: 4, 298, 311, 569 and complements thereof. Specification at page 43, line 13 through page 45, line 4. The claimed subject matter is also directed to a substantially purified nucleic acid molecule that encodes a maize transketolase enzyme or fragment thereof comprising a nucleic acid sequence of SEQ ID NO: 356 or complement thereof. Specification at page 18, lines 12-15. The claimed subject matter is also directed to an isolated nucleic acid molecule, where the nucleic acid molecule consists of a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 1, 4, 14, 27, 225, 298, 311, 356, 569, and 619 or complements thereof. Specification at page 45, lines 5-19.

6. Grounds of Rejection to be Reviewed on Appeal

The grounds of rejection to be reviewed in this Appeal are:

(a) claims 1, 2, 10-13, 15-22 and 24-31 stand rejected under 35 U.S.C. § 101 for allegedly being unsupported by a specific asserted utility or a well established utility;

(b) claims 1, 2 10-13, 15-22 and 24-31 stand rejected under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement because the claimed invention purportedly lacks utility;

(c) claims 1-2, 22 and 24-25 stand rejected under 35 U.S.C. § 112, first paragraph, for alleged failure to comply with the enablement requirement, and

(d) claims 1, 2 10-13, 15-22 and 24-30 stand rejected under 35 U.S.C. §112, first paragraph, for alleged insufficiency of written description.

A. Grouping of Claims

Claims 1, 2 10-13, 15-22 and 24-31 remain in this case. Claims 1, 10, 11, 22, 24, 26, 28 and 31 are independent. All of the claims at issue do not stand or fall together and the separate patentability of claims 1, 10, 11, 22, 24, 26, 28 and 31 is particularly

addressed in Sections 7.B(1)(d) and 7.E(3), (4) and (5) below. A copy of the claims on appeal is attached hereto as Appendix A.

7. Argument

A. Summary of Appellant's Position

As the Supreme Court said in *Brenner v. Manson*, the "basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility...where specific benefit exists in currently available form." 383 U.S. 519, 534-35, 148 U.S.P.Q. 689, 695 (1966). Appellant has met their part of the bargain – they have disclosed nucleic acid molecules which, in their current form, provide at least one specific benefit to the public, for example use to identify the presence or absence of a polymorphism in a population of soybean or maize plants. This benefit is specific, not vague or unknown, and it is a "real world" or substantial benefit. Because the claimed nucleic acid molecules provide at least these benefits, they satisfy the utility requirement of 35 U.S.C. § 101. Because the specification teaches how to make and use the claimed nucleic acid molecules for the disclosed utilities, the enablement requirement of 35 U.S.C. § 112 has been met.

Furthermore, Appellant has provided an adequate description of the claimed nucleic acid molecules that demonstrates Appellant's possession of the claimed invention. The genera of claimed nucleic acid molecules, for example, the genus of nucleic acid molecules comprising the nucleic acid sequence of SEQ ID NOs: 1, 4, 14, 27, 225, 298, 311, 356, 569, 619 and complements thereof have been described by the recitation of common structural features, *e.g.*, the nucleotide sequence of SEQ ID NO: 1, 4, 14, 27, 225, 298, 311, 356, 569, and 619, which distinguish molecules in the claimed genera from molecules not in the claimed genera. Because the specification demonstrates that Appellant had possession of (and have provided an adequate description of) the

claimed genera of nucleic acid molecules, the specification satisfies the written description requirement of 35 U.S.C. § 112.

B. The Claimed Nucleic Acids Have Legal Utility

Claims 1, 2 10-13, 15-22 and 24-31 stand rejected under 35 U.S.C. § 101 as allegedly "not supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility." Final Action mailed April 12, 2004 ("Final Action"), at page 2.

The Examiner acknowledges that the specification describes multiple utilities for the present invention, including "to obtain nucleic acids from other species, to isolate promoters, to detect/identify polymorphisms, in genetic mapping, as molecular markers, to follow expression (e.g. to create an Expression Response), in hybridization experiments, and in tissue printing." Office Action mailed June 17, 2003 at page 3. However, the Examiner asserts these utilities are not specific because the disclosed uses "are generic to the class of nucleic acids." Final Action., at page 2. The Examiner also asserts that further research would be required to confirm a 'real world' use. *Id.*, at pages 2-4.

This analysis misstates the nature of the asserted uses, ignores disclosed utilities, and misapplies the doctrine of "practical utility" developed by the courts after *Brenner v. Manson*. The "threshold for utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." *Juicy Whip, Inc. v. Orange Bang, Inc.*, 185 F.3d 1364, 1366, 51 U.S.P.Q.2d 1700, 1702 (Fed. Cir. 1999), *citing Brenner v. Manson*, 383 U.S. 519, 534 (1966). Furthermore, an invention need only provide <u>one</u> identifiable benefit to satisfy 35 U.S.C. § 101. *See Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983) ("when a properly claimed invention meets at least one stated objective, utility under section 101 is clearly shown").

The courts have expressed a test for utility that hinges on whether an invention provides an "identifiable benefit." *Juicy Whip*, 185 F.3d at 1366, 51 USPQ.2d at 1702. For analytical purposes, the requirement for an "identifiable benefit" may be broken into two prongs: (1) the invention must have a specific, *i.e.*, not vague or unknown benefit, *In re Brana*, 51 F.3d 1560, 1565, 34 U.S.P.Q.2d 1436, 1440 (Fed. Cir. 1995); and (2) the invention must provide a real world, *i.e.*, practical or "substantial" benefit. *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1563, 39 U.S.P.Q.2d 1895, 1899 (Fed. Cir. 1996). A corollary to this test for utility is that the invention must not be "totally incapable of achieving a useful result," *i.e.*, the utility must not be incredible or unbelievable. *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, 24 U.S.P.Q.2d 1401, 1412 (Fed. Cir. 1992).

Applicants have asserted in the specification that the claimed nucleic acid molecules provide identifiable benefits, for example, use as nucleic acid molecule markers and probes (*see, e.g.,* specification at page 79, line 18 through page 80, line 5); to identify and obtain nucleic acid homologues (*see, e.g.,* specification at page 64, line 10 through page 65, line 20); in microarrays as gene-specific targets (*see, e.g.,* specification at page 85, line 6 through page 87, line 11); to identify the presence or absence of a polymorphism (*see, e.g.,* specification at page 67, line 3 through page 74, line 18); use to transform plants (*see, e.g.,* specification at page 92, line 1 through page 110, line 16); to determine the level or pattern of expression of a protein or mRNA associated with that nucleic acid molecule (*see, e.g.,* specification at page 80, line 6 through page 85, line 5); and use to overexpress or suppress a desired protein (*see, e.g.,* specification at page 110, line 12 through page 113, line 4). Any of these utilities described alone is enough to satisfy Section 101. Because Applicants need only establish a single utility to satisfy 35 U.S.C. § 101, and have done so in the present case, the premise of the rejection under Section 101 is incorrect, and the rejection should be reversed.

(1) The Claimed Nucleic Acid Molecules Provide A Specific Benefit, *i.e.*, They Have Specific Utility

The Examiner acknowledges that the specification describes multiple utilities for the present invention, including "to obtain nucleic acids from other species, to isolate promoters, to detect/identify polymorphisms, in genetic mapping, ... in hybridization experiments, and in tissue printing." Office Action mailed June 17, 2003 at page 3. Moreover, the specification also discloses additional utilities for the claimed nucleic acid molecules,[1] including use of the claimed nucleic acid molecules to measure the level of mRNA in a sample,[2] and use as molecular markers.[3]

(a) Identifying the Presence or Absence of a Polymorphism

For example, one of the utilities disclosed in the specification is use of the claimed nucleic acid molecules to identify the presence or absence of a polymorphism. Specification at page 67, line 3 through page 74, line 18. The Examiner argues that this utility, like many of the asserted utilities, is not specific or substantial, *see, e.g.,* Final Action at page 2, but does not provide any support (legal or factual) for the proposition that detection of polymorphisms using the claimed nucleic acid molecules is not a legal utility.

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[1] It is irrelevant whether the corresponding mRNA or polypeptide have utility because Applicants are not relying solely on utility of the mRNA or polypeptide to establish utility of the claimed nucleic acid molecules.

[2] It is standard practice to screen populations of nucleic acids with EST sequences, often attached to a microarray, without characterizing each and every target mRNA. Knowing that the gene corresponding to the claimed nucleic acid molecules is expressed under certain conditions or in certain tissues or at certain levels is in itself useful. For example, such information is useful to detect expression changes in traits of interest, *e.g.*, genes involved in the phosphogluconate pathway.

[3] One can use the claimed nucleic acid molecules to determine location of a corresponding DNA sequence on a physical map or genetic map location without knowing anything beyond the claimed sequence. The use of molecular markers is a practical activity in the development of nutritionally enhanced or agriculturally enhanced crops. Such markers are useful in, for example, genetic mapping or linkage analysis, marker-assisted breeding, physical genome mapping, transgenic crop production, crop monitoring diagnostics, and gene identification and isolation. As more markers are identified, genetic maps will become more detailed and it will be easier for plant breeders to breed for particular traits.

Many of the disclosed utilities in this case, including the detection of polymorphisms, are directly analogous to the utilities of a microscope, *i.e.*, the claimed nucleic acid molecules may be used to locate and measure nucleic acid molecules within a sample, cell, or organism. The Examiner denigrates such utilities by asserting that these utilities are not "useful" because "none of the claimed sequences are disclosed as having a polymorphic site, or as being known to be associated with a polymorphism." Final Action, at page 2. However, the fact that, *e.g.*, a new and nonobvious microscope or screening assay can be used for learning about products or processes does not lessen the fact that such "tools" have legal utility. "Many research tools such as gas chromatographs, screening assays, and nucleotide sequencing techniques have clear, specific and unquestionable utility (*e.g.*, they are useful in analyzing compounds)." MPEP § 2107.01 at page 2100-33.

Use of the claimed nucleic acid molecules to detect the presence or absence of polymorphisms is no more legally insufficient than using a gas chromatograph to analyze the chemical composition of a gas – such use determines information about the gas, not the gas chromatograph. Even if the gas chromatograph detects the absence of a particular chemical element in the gas, that finding does not obviate the utility of the gas chromatograph itself. Information has been obtained about the gas.[4] Likewise, the claimed nucleic acid molecules have utility even if the absence of a particular polymorphism is detected. Indeed, the absence of a polymorphism usefully demonstrates that the two (or more) populations being compared share a common genetic heritage.

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[4] For example, gas sampled from crude oil may be analyzed by gas chromatography for the presence or absence of chlorine, which is toxic to catalysts used in gasoline refining even in very low concentrations. The absence of a peak at the molecular weight of chlorine indicates the absence of chlorine in the sample being tested, thereby providing useful information (no chlorine is present, therefore the catalyst will not be destroyed) to the refinery manager. *See, e.g.*, U.S. Patent No. 6,133,740 entitled "Chlorine Specific Gas Chromatographic Detector."

The claimed nucleic acid molecules have been asserted to work for a specific, *i.e.*, not vague or unknown benefit, to identify the presence or absence of a polymorphism. This benefit is immediately realized directly from the use of the claimed nucleic acids, not from the use of other molecules. Such a proven use that provides an acknowledged known benefit to the public satisfies the utility requirement of 35 U.S.C. § 101.

(b) Probes for Other Molecules or Source for Primers

Other uses for the claimed nucleic acid molecules are as probes for other molecules or as a source of primers. The Examiner suggests that these uses are not legal utilities because "a 'use' to do further research is not a specific, substantial and credible utility under 35 USC 101." Final Action, at pages 2. This is not correct. The specification discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms such as alfalfa, *Arabidopsis*, barley, *Brassica*..., sunflower, oil palm, and *Phaseolus*, etc.[5] Specification at page 47, line 21 through page 48, line 3. The Examiner has not provided any evidence that would reasonably suggest that this cannot be done, and thus has not met the burden of proof required to establish a utility rejection. *See In re Brana*, 51 F.3d 1560, 1567, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995). *Accord In re Gaubert*, 524 F.2d 1222, 1225-26, 187 U.S.P.Q. 664, 666 (C.C.P.A. 1975); *In re Langer*, 503 F.2d 1380, 1391, 183 U.S.P.Q. 288, 297 (C.C.P.A. 1974).

One illustrative example of a molecule that can be isolated using a claimed nucleic acid molecule is the promoter of the gene corresponding to that claimed nucleic acid molecule. Applicants have specifically disclosed that one use of the claimed nucleic

[5] Furthermore, one skilled in the art of hybridization and amplification understands how to design and utilize probes and primers to target a sequence of interest, and therefore it is not necessary for Applicants to provide a laundry list of each and every nucleic acid molecule that can be identified using the claimed nucleic acid molecules.

acid molecules is to initiate a chromosome walk or alternatively in chromosome landing. Specification at page 65, line 21, through page 66, line 10. The Examiner denigrates that utility by asserting that it is not specific because it is generally applicable to any nucleic acid. Final Action at pages 2-3. This is not correct. The claimed nucleic acid molecules are particularly useful, for example, to identify markers and isolate promoters in soybean plants. *See, e.g.*, specification at page 65, line 3 through page 67, line 2 and page 152, line 14 through page 219, line 22.

In short, the Examiner suggests that the asserted utilities are legally insufficient simply because other molecules can be used for the same purpose, *e.g.*, chromosome walks. That position is wrong as a matter of law – there is no requirement of exclusive utility in the patent law. *See Carl Zeiss Stiftung v. Renishaw PLC*, 945 F.2d 1173, 1180, 20 U.S.P.Q.2d 1094, 1100 (Fed. Cir. 1991) ("An invention need not be the best or the only way to accomplish a certain result..."). Such an argument would imply that a new golf club has no legal utility because other golf clubs can be used for the same purpose, *i.e.*, hitting golf balls. That position must be rejected as it requires reading "into the patent laws limitations and conditions which the legislature has not expressed," a practice condemned by the Supreme Court. *See Diamond v. Chakrabarty*, 447 U.S. 303, 308, 206 U.S.P.Q. 193, 196 (1980), *quoting United States v. Dubilier Condenser Corp.*, 289 U.S. 178, 199, 17 U.S.P.Q. 154, 162 (1933).

Moreover, it is factually incorrect that this use is not "specific" to the claimed nucleic acid molecules. The claimed nucleic acid molecules provide a particularly appropriate and demonstrably useful starting point for a walk to isolate promoters in maize and soybean plants. *See, e.g.*, specification at page 65, line 21 through page 67, line 2. A random nucleic acid molecule does not provide an equally good starting point to isolate such genes. Furthermore, even if a random nucleic acid molecule provided a better starting point than the claimed nucleic acid molecules, it would not obviate the

utility of the claimed nucleic acid molecules. An invention may be "less effective than existing devices but nevertheless meet the statutory criteria for patentability." *Custom Accessories, Inc. v. Jeffrey-Allan Indus.*, 807 F.2d 955, 960 n.12, 1 U.S.P.Q.2d 1196, 1199 n.12 (Fed. Cir. 1986).

The Examiner has failed to provide evidence, or even to suggest a reason for believing that the claimed nucleic acid molecules could not be so used. Accordingly, the assertion of this utility as a probe for other molecules or as a source of primers satisfies the requirements of 35 U.S.C. § 101. *See In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995).

(c) Use to Encode Phosphogluconate Pathway Enzymes

One of the utilities disclosed in the specification is use of the claimed nucleic acid molecules to encode enzymes involved in the phosphogluconate pathway or fragments thereof. *See, e.g.,* Specification at page 46, line 6, through page 52, line 16, page 222, line 8 through page 223, line 13 and Table A. The Examiner argues that this utility is not specific or substantial, because "the specification does not actually disclose that any of the claimed SEQ ID NO's is known to encode a protein or peptide, specifically one of the enzymes recited in the claims." Final Action at page 3. However, the Examiner provides no support to show that the claimed SEQ ID NOs do not function as described by the specification.

The specification provides extensive evidence based on sequence identity that the claimed nucleic acid molecules encode enzymes of the phosphogluconate pathway. *See, e.g.,* specification at page 224 (Table A). The specification also indicates by way of EC classification designations that the specified enzymes are of an enzymatic classification well-known in the art. *See, e.g.,* specification at page 2, line 12 through page 4, line 20.

Further, a detailed description of the characterization of the specified enzyme, as well as the identification of such enzyme from other sources is provided in the specification. *Id.*

An examiner must accept a utility by an applicant unless the Office has evidence or sound scientific reasoning to rebut the assertion. *See In re Oetiker*, 977 F.2d 1443, 1445, 24 U.S.P.Q.2d 1443, 1444 (Fed. Cir. 1992). "More specifically, when a patent application claiming a nucleic acid asserts a specific, substantial, and credible utility, and bases the assertion upon homology to existing nucleic acids or proteins having an accepted utility, the asserted utility must be accepted by the examiner unless the Office has sufficient evidence or sound scientific reasoning to rebut such as assertion." Federal Register 66(4):1096, Utility Guidelines (2001). "[A] 'rigorous correlation' need not be shown in order to establish practical utility; 'reasonable correlation' is sufficient." *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1565, 39 U.S.P.Q.2d 1895, 1900 (Fed. Cir. 1996).

The claimed nucleic acid molecules have been asserted to encode phosphogluconate pathway enzymes or fragments thereof. The specification provides ample correlation between the claimed nucleic acid molecules and phosphogluconate pathway enzymes. Accordingly, the assertion of the use of the claimed nucleic acid molecules to encode phosphogluconate pathway enzymes or fragments thereof satisfies the utility requirement of 35 U.S.C. § 101.

(d) Claims 10-21, 26-27 and 29-31 are separately patentable

As discussed above, the Examiner has rejected the claims as allegedly lacking utility because "the specification does not actually disclose that any of the claimed SEQ ID NO's is known to encode a protein or peptide." Final Action at page 3-3. However, claims 10-21, 26-27 and 29-31 are directed to isolated nucleic acid molecules that hybridize to, or comprise, recited SEQ ID NOs. Even if such a basis for rejection was proper, it would not apply to claims 10-21, 26-27 and 29-31 which do not recite nucleic

acid molecules that "encodes a maize or soybean" phospholuconate pathway enzyme. Applicants have provided a specific utility for the claimed invention. That is all that is required.

(2) The Claimed Nucleic Acid Molecules Provide Practical, Real World Benefits, *i.e.*, They Have Substantial Utility

The Final Action also appears to assert that the disclosed uses are legally insufficient because they are not "substantial" utilities. Final Action at pages 2-4. The touchstone of "substantial" utility is "real world" or "practical utility." *See, e.g., Fujikawa v. Wattanasin*, 93 F.3d 1559, 1563, 39 U.S.P.Q.2d 1895, 1899 (Fed. Cir. 1996). " 'Practical utility' is a shorthand way of attributing 'real world' value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public." *Nelson v. Bowler*, 626 F.2d 853, 856, 857, 206 U.S.P.Q. 881, 883 (C.C.P.A. 1980) ("tests evidencing pharmacological activity may manifest a practical utility even though they may not establish a specific therapeutic use").[6]

There can be no question that one skilled in the art can use the claimed nucleic acid molecules in a manner which provides an immediate benefit to the public, for example to detect the presence or absence of polymorphisms. The detection of polymorphisms provides an immediate benefit to the public because, *e.g.*, it enables a plant breeder to determine the distribution of parental genetic material in the progeny of a cross. This information about a plant's genetic profile, like the information about a compound's pharmacological profile in *Nelson*, provides an immediate benefit and thus a practical utility to the public.

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[6] *Accord Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 U.S.P.Q. 739, 747-48 (Fed. Cir. 1985); *Rey-Bellet v. Engelhardt*, 493 F.2d 1380, 1383, 181 U.S.P.Q. 453, 454 (C.C.P.A. 1974).

Quite apart from the detection of polymorphisms, there is also no question that the public has recognized the benefits provided by the claimed subject matter, and has attributed "real world" value to such nucleic acid molecules. The utility of ESTs is not merely an academic issue; the real world value of these constructs is self-evident from the growth of a multi-million dollar industry in the United States premised on their usefulness. Like fermentation processes involving bacteria, ESTs and nucleic acid molecules with EST sequences are "industrial product[s] used in an industrial process – a useful or technical art if there ever was one." *In re Bergy*, 563 F.2d 1031, 1038, 195 U.S.P.Q. 344, 350 (C.C.P.A. 1977).

The market participants for EST products are primarily sophisticated corporations and highly knowledgeable scientists who are unlikely to pay for useless inventions. *Cf. Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 960, 220 U.S.P.Q. 592, 599 (Fed. Cir. 1983) ("People rarely, if ever, appropriate useless inventions"). Quite simply, the commercial value of these products is proof of their real world value and of the benefits they provide to the public. This evidence cannot be ignored. The patent system was created to serve and foster growth and development in the industrial arts. If the industries themselves recognize and appreciate the value of an invention, it is not for the Patent Office to say that they are mistaken.

(3) The Disclosed Utilities Are Credible to One of Skill in the Art

An assertion of utility must be accepted by the Examiner unless it would not be considered "credible" by a person of ordinary skill in the art. MPEP § 2107 at 2100-29. Cases in which utility was found not to be credible are rare, and usually involve "hare-brained" utilities.[7] A challenge to the credibility of a utility is essentially a challenge

[7] Examples of incredible utilities are given in MPEP § 2107.01 at page 2100-34, and include:

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directed to operability, and such a challenge must be supported by a clear statement of "factual reasons which would lead one skilled in the art to question the objective truth of the statement of operability." *In re Gaubert*, 524 F.2d 1222, 1225-26, 187 U.S.P.Q. 664, 666 (C.C.P.A. 1975); *see In re Brana*, 51 F.3d 1560, 1567, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995); MPEP § 2107.02 at 2100-41.

Applicants have explicitly identified specific and substantial utilities, not only in the specification, but in Applicants' Response dated February 19, 2002, at pages 8-11 and in Applicants' Response dated January 7, 2003, at pages 6-10. "To violate [35 U.S.C.] 101 the claimed device must be totally incapable of achieving a useful result." *Brooktree Corp. v. Advanced Micro Devices, Inc.*, 977 F.2d 1555, 1571, 24 U.S.P.Q.2d 1401, 1412 (Fed. Cir. 1992). To date, the Examiner has provided no evidence that the claimed nucleic acid molecules will not work for the disclosed utilities. Unless and until the Examiner can prove that the claimed invention is wholly inoperative, the rejection must be withdrawn.

In view of the above, Applicants contend that the claimed nucleic acid molecules are supported by credible, specific, and substantial utilities disclosed in the specification. Moreover, the Examiner has failed to raise any credible evidence challenging the

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an invention asserted to change the taste of food using a magnetic field (*Fregeau v. Mossinghoff*, 776 F.2d 1034, 227 U.S.P.Q. 848 (Fed. Cir. 1985)), a perpetual motion machine (*Newman v. Quigg*, 877 F.2d 1575, 11 U.S.P.Q. 1340 (Fed. Cir. 1989)), a flying machine operating on "flapping or flutter function" (*In re Houghton*, 433 F.2d 820, 167 U.S.P.Q. 687 (C.C.P.A. 1970)), a method for increasing the energy output of fossil fuels upon combustion through exposure to a magnetic field (*In re Ruskin*, 354 F.2d 395, 148 U.S.P.Q. 221 (C.C.P.A. 1966)), uncharacterized compositions for curing a wide array of cancers (*In re Citron*, 325 F.2d 248, 139 U.S.P.Q. 516 (C.C.P.A. 1963)), a method of controlling the aging process (*In re Eltgroth*, 419 F.2d 918, 164 U.S.P.Q. 221 (C.C.P.A. 1970)), and a method of restoring hair growth (*In re Ferens*, 417 F.2d 1072, 163 U.S.P.Q. 609 (C.C.P.A. 1969)).

presently asserted utilities. Consequently, the rejection of claims 1, 2 10-13, 15-22 and 24-31 under 35 U.S.C. §101 is improper and should be reversed.

C. The Claimed Nucleic Acids Are Enabled by the Specification

The enablement of the claimed nucleic acid molecules has been challenged. Claims 1, 2 10-13, 15-22 and 24-31 stand rejected as not enabled by the specification, because the claimed nucleic acid molecules allegedly lack utility and therefore cannot be enabled. Final Action at page 4. This rejection is erroneous and has been overcome by the arguments stated above regarding utility because it is well-established law that "the enablement requirement is met if the description enables any mode of making and using the invention." *Johns Hopkins University v. CellPro*, 152 F.3d 1342, 1361, 47 U.S.P.Q.2d 1705, 1719 (Fed. Cir. 1998) (emphasis added), *quoting Engel Indus. v. Lockformer Co.*, 946 F.2d 1528, 1533, 20 U.S.P.Q.2d 1300, 1304 (Fed. Cir. 1991). Unless and until the Examiner comes forth with evidence to rebut the objective truth of the utilities disclosed in the specification, this enablement rejection must be withdrawn as improper. *See In re Wright*, 999 F.2d 1557, 1561-62, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993); *Ex parte Lemak*, 210 U.S.P.Q. 306, 307 (Bd. App. 1981) ("pure conjecture" does not substantiate rejection for lack of enablement).

D. The Skilled Artisan can Practice the Claimed Invention Without Undue Burden

In addition, claims 1-2, 22 and 24-25 stand rejected under 35 U.S.C. §112, first paragraph because the claims allegedly "contains subject matter which was not described in the specification in such a way as to enable one skilled in the art... to make and use the invention." Final Action at page 5. The Examiner alleges that "due to uncertainty in the art for how to synthesize or express any active enzyme from a nucleic acid not known to actually encode that enzyme, and the lack of teaching in the specification for how to test

for the particular activities claimed once any peptide putatively encoded IS synthesized, the specification does not provide an enabling disclosure for claims directed to nucleic acids encoding recited enzymes." *Id.* at page 6. However, no analysis of the factors set forth in *In re Wands* has been presented by the Examiner. To the contrary, Appellant asserts that an analysis of the criteria presented by *In re Wands* supports Appellant's position that no undue experimentation would be required to make and use the claimed invention for the uses disclosed in the specification. *See In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1998).

The first *Wands* criterion is the quantity of experimentation necessary. The "make-and-test" quantum of experimentation is reduced by the extensive knowledge, *e.g.*, of conservative nucleotide substitutions, identification of an active site, and conserved regulatory elements, to which a person of ordinary skill in the art has access. The Examiner generally asserts that undue experimentation would be required by the skilled artisan to use the instant invention. Final Action at pages 5-6. However, one skilled in the art is sufficiently guided by Applicants' disclosure, which sets forth nucleic acid molecules obtained from cDNA libraries, sequence alignment results and enzyme characterization. Further, performing routine and well-known steps, such as sequence alignment protocols, transformations and gene expression analysis, cannot create undue experimentation even if it is laborious. *See In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 218-219 (C.C.P.A. 1976).

The second and third *Wands* criteria relate to the amount of direction or guidance given, and the presence or absence of working examples. Again, the specification provides evidence of sequence identity and hybridization conditions, discusses the use of the claimed nucleic acid molecules in the phosphogluconate pathway and discusses the use of the claimed nucleic acid sequence to isolate additional sequences within a genome. *See, e.g.,* Specification at pages 61, line 1 through page 67, line 2, page 152, line 14

through page 223, line 13 (Examples 1-4), the sequence listing and Table A. Based on such disclosure, one of ordinary skill in the art would be enabled to make and use the invention commensurate in scope with the claims.

The fourth, fifth, and sixth *Wands* criteria focuses on the nature of the invention, the state of the art, and the relative skill in the art. The specification provides a detailed description of the nucleic acid sequences required by the claims, and further describes the preparation of constructs and methods of use related thereto. *See, e.g.*, specification at page 46, line 6 through page 52, line 16, and Table A (describing nucleic acid molecules of the present invention as encoding phosphogluconate pathway enzymes), and page 92, line 1 through page 146, line 4 (describing use of the claimed nucleic acid molecules in the preparation of expression vectors and expression systems). Practitioners in this art are guided by considerable knowledge and resources on the conditions and approaches that can be utilized to identify, confirm, and introduce into other hosts, nucleic acid and amino acid sequences.

The seventh criterion considers the predictability of the art. Appellant respectfully asserts, as discussed *supra*, that the specification discloses sufficient guidance to render the results of transformations with the claimed nucleic acid molecules predictable. *See, e.g.,* specification at page 92, line 1 through page 146, line 4. Furthermore, the specification provides sufficient guidance to one of skill in the art to decipher the information necessary to make and use the claimed nucleic acid molecules. *See, e.g.,* specification at page 46, line 6 through page 52, line 16 (describing nucleic acid molecules and enzymes involved in the phosphogluconate pathway), and page 80, line 6 through page 86, line 19 (citing methods for assaying gene expression).

The eighth criterion focuses on the breadth of the claims. Enablement is satisfied when the disclosure "adequately guide[s] the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus

possess the disclosed utility". *See In re Vaeck,* 947 F.2d 488, 496, 20 U.S.P.Q.2d 1438, 1445 (Fed. Cir. 1991). In the present case, one of skill in the art is specifically guided by the disclosure to look to, *e.g.*, sequence identity data in making that determination.

The Examiner has not met the evidentiary burden to impose an enablement rejection. A specification that discloses how to use a claimed invention "must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein." *In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995), *quoting In re Marzocchi*, 439 F.2d 220, 223, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971) (emphasis in original).

The Examiner has provided neither evidence supporting the rejection nor any explanation of why the specification allegedly fails to enable the nucleic acid molecules of claims 1-2, 22 and 24-25. *See In re Wright*, 999 F.2d 1557, 1561-62, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993); *Ex parte Lemak*, 210 U.S.P.Q. 306, 307 (B.P.A.I. 1981) ("pure conjecture" does not substantiate rejection for lack of enablement). Therefore, because the above analysis illustrates that the specification clearly enables at least the methods of making and using the invention as set forth in the Examples, and the claims, the enablement requirement has been satisfied. *Cf. Johns Hopkins University v. CellPro*, 152 F.3d 1342, 1361, 47 U.S.P.Q.2d 1705, 1719 (Fed. Cir. 1998) ("the enablement requirement is met if the description enables any mode of making and using the invention") (emphasis added), *quoting Engel Indus. v. Lockformer Co.*, 946 F.2d 1528, 1533, 20 U.S.P.Q.2d 1300, 1304 (Fed. Cir. 1991). Accordingly, the rejection of claims 1-2, 22 and 24-25 under 35 U.S.C. § 112, first paragraph is improper and should be reversed.

E. The Specification Provides an Adequate Written Description of the Claimed Invention

Despite the Examiner's acknowledgement that the specification discloses the sequences of SEQ ID NOs: 1, 4, 14, 27, 225, 298, 311, 356, 569 and 619, the adequacy of the written description of claims 1, 2, 10-13, 15-22 and 24-30 has been challenged by the Examiner because the claimed subject matter was allegedly "not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." Final Action, at page 6. The basis for the Examiner's challenge is that "[a]s the sequences recited in the claims are apparently fragments which do not appear to comprise ORF's or actually encode any known proteins, a nucleic acid 'comprising' the fragments encompasses much larger sequences which may encode entirely difference proteins from those recited, encompasses genomic sequences which may also comprise introns, noncoding regions, etc." Final Action at page 7. The Examiner also argues that some of the pending claims "are specifically directed to encompass sequences that hybridize to the claimed SEQ ID NOs." *Id.* The Examiner further argues that the "specification sets forth a list of possible variations for the inventive sequences... but does not actually describe, by sequence or structure, any of the variations, nor does the specification disclose any longer sequences (e.g. genomic) which may comprise the claimed sequences." *Id.* The Examiner concludes that the "specification fails to describe any sequence which does not *consist* of a claimed SEQ ID NO." *Id.* at page 9. This is not a proper basis for a written description rejection of a "comprising" claim. If it was, every "comprising" claim ever written would be invalid for failing to describe every nuance of the claimed invention. Furthermore, the specification demonstrates to one skilled in the art that Appellant was in possession of the claimed genera of nucleic acid molecules.

(1) The Specification Reflects Appellant's Possession of the Claimed Invention

The purpose of the written description requirement is to ensure that the inventors had possession of the claimed subject matter, *i.e.*, to ensure that the inventors actually invented what is claimed. *Gentry Gallery Inc. v. Berkline Corp.*, 134 F.3d 1473, 1479, 45 U.S.P.Q.2d 1498, 1503 (Fed. Cir. 1998); *Lockwood v. American Airlines*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997); *In re Alton*, 76 F.3d 1168, 1172, 37 U.S.P.Q.2d 1578, 1581 (Fed. Cir. 1996). If a person of ordinary skill in the art would, after reading the specification, understand that the inventors had possession of the claimed invention, even if every nuance of the invention was not expressly described, then the written description requirement has been met. *In re Alton*, 76 F.3d at 1175, 37 U.S.P.Q.2d at 1584. After reading the present specification, a person of ordinary skill in the art would understand that Appellant had possession of the claimed nucleic acid molecules, and therefore, the claimed invention.

Appellant has provided the nucleic acid sequence required by the claims, *i.e.*, SEQ ID NOs: 1, 4, 14, 27, 225, 298, 311, 356, 569 and 619 as well as, for example, vectors comprising the nucleic acid sequence (*see, e.g.*, specification 93, line 1 through page 107, line 19), appropriate hybridization conditions (*see, e.g.*, specification at page 43, line 13 through page 45, line 4) ; nucleic acid molecules comprising nucleic acid sequences having conservative variations or encoding amino acid sequences having conservative substitutions (*see, e.g.*, specification at page 48, line 6 through page 50, line 6); fusion protein or peptide molecules or fragments thereof encoded by the nucleic acid molecules of the present invention (*see, e.g.*, specification at page 59, lines 4-15); plant homologue proteins (*see, e.g.*, specification at page 59, line 16 through page 60, line 6); site directed mutagenesis of the claimed nucleic acid molecules (*see, e.g.*, specification at page 87, line 12 through page 89, line 3); and construction of cDNA libraries using the claimed nucleic acid molecules (*see, e.g.*, specification at page 152, line 13 through page

222, line 7 (Examples 1-3)). The fact that the claims at issue are intended to cover molecules that include the recited sequence joined with additional sequences, or to cover sequences that specifically hybridize under the recited conditions, does not mean that Appellant was any less in possession of the claimed nucleic acid molecules.[8] It is well-established that use of the transitional term "comprising" leaves the claims "open for the inclusion of unspecified ingredients even in major amounts." *Ex parte Davis*, 80 U.S.P.Q. 448, 450 (B.P.A.I. 1948). *Accord PPG Indus. v. Guardian Indus.*, 156 F.3d 1351, 1354, 48 U.S.P.Q.2d 1351, 1353-54 (Fed. Cir. 1998); *Moleculon Research Corp. v. CBS*, 793 F.2d 1261, 1271, 229 U.S.P.Q. 805, 812 (Fed. Cir. 1986).

Appellant has provided in the present disclosure not only the nucleotide sequence required by the claims (i.e. SEQ ID NOs: 1, 4, 14, 27, 225, 298, 311, 356, 569 and 619), but also several variations including and directed to the claimed nucleic acid molecules. For example, as described above, the present specification describes vectors comprising the claimed nucleic acid molecules (specification at page 93, line 1 through page 146, line 4), and describes how to make the nucleotide sequences and libraries from which they were originally purified. *See, e.g.*, Examples page 152, line 14, *et. seq.* Furthermore, the addition of extra nucleotides or detectable labels to the disclosed nucleotide sequences (SEQ ID NOs: 1, 4, 14, 27, 225, 298,311, 356, 569 and 619) is readily envisioned by one of ordinary skill in the art upon reading the present specification,[9] in particular at page 59, lines 4-15 (describing fusion peptide molecules

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[8] If the Examiner is arguing that no possession is shown because the precise claim language is not used in the specification, then she goes beyond what is required by the law. It is well-settled that the description of a claimed invention need not be *in ipsis verbis*. *Gentry Gallery v. Berkline Corp.*, 134 F.3d 1473, 1479, 45 U.S.P.Q.2d 1498, 1503 (Fed. Cir. 1998); *In re Alton*, 76 F.3d 1168, 1175, 37 U.S.P.Q.2d 1578, 1583 (Fed. Cir. 1996); *Martin v. Johnson*, 454 F.2d 746, 751, 172 U.S.P.Q. 391, 395 (C.C.P.A. 1972).

[9] It is established patent jurisprudence that Applicants need not teach "conventional and well-known genetic engineering techniques." *E.g., Ajinomoto Co. v. Archer-Daniels-Midland Co.*, 228 F.3d 1338, 1345, 56 U.S.P.Q.2d 1332, 1337 (Fed. Cir. 2000).

encoded by the claimed nucleic acid molecules), page 43, lines 1-5 (describing sequences with labels to facilitate detection), page 87, line 12 through page 89, line 3 (describing site-directed mutagenesis) and page 145, line 20 through page 146, line 4 (citing references describing the construction, manipulation and isolation of nucleic acid macromolecules).

In addition, as described above, the present specification also describes nucleic acid sequences that hybridize to the claimed SEQ ID NOs. *See, e.g.*, Specification at page 43, line 13 through page 45, line 4. The specification also describes nucleic acid molecules comprising nucleic acid sequences having conservative variations or encoding amino acid sequences having conservative substitutions (*see, e.g.*, specification at page 48, line 6 through page 50, line 6); plant homologue proteins (*see, e.g.*, specification at page 59, line 16 through page 60, line 6); and site directed mutagenesis of the claimed nucleic acid molecules (*see, e.g.*, specification at page 87, line 12 through page 89, line 3).

Moreover, the court determined, in *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 1321, 63 U.S.P.Q.2d 1609, 1610 (Fed. Cir. 2002), that the written description inquiry is a factual one determined on a case-by-case basis and that, in a given disclosure, "it may well be that various subsequences, mutations, and mixtures of those sequences are also described to one of skill in the art." *Enzo*, 296 F.3d at 1326-1327, 63 U.S.P.Q.2d at 1615. Furthermore, it is well established that claims "may be broader than the specific embodiment disclosed in a specification. *Ralston-Purina Co. v. Far-mor-Co*, 772 F.2d 1570, 1575, 227 U.S.P.Q. 177, 179 (Fed. Cir. 1985) (*quoting In re Rasmussen*, 650 F.2d 1212, 1215, 211 U.S.P.Q. 323, 326 (C.C.P.A. 1981).

(2) Appellant Has Described the Claimed Invention

The Final Action asserts that the "specification sets forth a list of possible variations for the inventive sequences... but does not actually describe, by sequence or structure, any of the variations, nor does the specification disclose any longer sequences (e.g. genomic) which may comprise the claimed sequences." Final Action at page 7. The Examiner appears to assert that each nucleic acid molecule within the claimed genus must be described by its complete structure. These assertions are totally unfounded. The Federal Circuit has elucidated a test for written description wherein a genus of nucleic acids may be described by a structural feature that distinguishes members of the claimed genus from non-members of the claimed genus. *Regents of the University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1568-69, 43 U.S.P.Q.2d 1398, 1406 (Fed. Cir. 1997). Appellant has satisfied that test for written description.

In particular, Appellant has disclosed structural features, for example, the nucleic acid sequences of SEQ ID NOs: 1, 4, 14, 27, 225, 298, 311, 356, 569, and 619, and their complements, as well as recited specific hybridization conditions. The common structural feature (the nucleotide sequence of SEQ ID NOs: 1, 4, 14, 27, 225, 298, 311, 356, 569, 619 and their complements) is shared by every nucleic acid molecule in the claimed genera, and this feature distinguishes members of the claimed genera from non-members. For example, if a nucleic acid molecule such as an mRNA contains the nucleotide sequence of SEQ ID NO: 1, then it is a member of the claimed genus of nucleic acid molecules comprising a nucleic acid sequence of SEQ ID NO: 1.[10] If a nucleic acid molecule does not contain SEQ ID NO: 1, then it is not a member of that claimed genus. The presence of other nucleotides at either end of the recited sequence

[10] The same argument applies with equal force to every genus of the claimed nucleic acid molecules. For example, if a nucleic acid molecule such as an mRNA comprises the nucleotide sequence of SEQ ID NO: 4, then it is a member of the claimed genus of nucleic acid molecules comprising a nucleic acid sequence of SEQ ID NO: 4. *See, e.g.*, claim 13.

will not interfere with the recognition of a claimed nucleic acid molecule as such – it either contains the nucleotides of SEQ ID NO: 1 or it does not. One skilled in the art, after reading the present specification, would clearly know if a nucleic acid molecule contains the recited nucleotide sequence.

Moreover, closely related nucleic acid molecules falling within the scope of the present claims are readily identifiable - they either hybridize under the claimed conditions to SEQ ID NOs: 1, 4, 14, 27, 225, 298, 311, 356, 569 and 619 (or complements thereof) or they do not. The fact that the nucleic acid molecules may comprise additional sequences or variations is beside the point. Such modifications are readily envisioned by one of ordinary skill in the art and disclosed throughout the specification.

Furthermore, nucleic acid molecules within the scope of the instant claims are also readily identifiable as they either encode a maize or soybean phosphogluconate pathway enzyme or fragment thereof or they do not. Claims 1-2, 22, 24, and 25 are directed to "substantially purified nucleic acid molecules that encode a maize or soybean" phosphogluconate pathway enzyme or fragment thereof. The specification describes nucleic acid sequences that encode maize or soybean phosphogluconate pathway enzymes or fragments thereof. *See, e.g.*, specification at page 152, line 13 through page 223, line 13 (Examples 1-4) and page 224, line 1, *et seq.* (Table A). Descriptions of ORFs are not required to comply with the written description requirement.

The Examiner relies on Baker, *et al. Protein Structure Prediction and Structural Genomics*, *Science*, Vol. 294 (Oct. 5, 2001), pp 93-96 to support the allegation "that structural (de novo) models are more accurate at predicting functional homologies between proteins, especially where sequence comparison fails." Final Action at page 9. The Examiner would require a "comparison of binding regions, conserved regions, catalytic regions, etc. to support that the peptides putatively encoded by the claimed SEQ ID NOs would be expected to actually exhibit" enzyme activity. Final Action at page 9.

Such a requirement is beyond the written description requirement. The Examiner has offered no evidence to demonstrate, in light of Appellant's disclosure, why one of ordinary skill in the art would reasonably doubt that a nucleic acid molecule comprising a nucleic acid sequence of SEQ ID NOs: 1, 4, 14, 27, 225, 298, 311, 356, 569, 619 or the complements thereof would encode a maize or soybean phosphogluconate pathway enzyme or fragment thereof and, as such, has not met the burden to impose a written description rejection. Appellant has described nucleic molecules that encode phosphogluconate pathway enzymes or a fragment thereof. *See, e.g.*, Table A. That is all that is required under 35 U.S.C. § 112, first paragraph.

(3) Claims 10, 11-21 and 26-30 are separately patentable

The Examiner argues that "[t]he specification fails to describe ANY nucleic acid actually encoding one or more of the claimed enzymes." Final Action at page 10. The Examiner provides no support as to why one of skill in the art would not be able to recognize a nucleic acid molecule that encodes a maize or soybean phosphogluconate pathway enyzme comprising a nucleic acid sequence that hybridizes to a nucleic acid sequence of SEQ ID NOs: 1, 4, 14, 225, 298, 311, 569 and 619 or complements thereof. The specification describes the claimed sequences and hybridization conditions. *See, e.g.*, specification at page 43, line 13 through page 45, line 4 and in the sequence listing and Table A. The skilled artisan would recognize that Appellant had possession of a nucleic acid sequence encoding the recited enzymes comprising the claimed SEQ ID NOs, as well as complements and variations thereof. Moreover, such a basis for rejection, even if valid, would not apply to claims 10, 11-21 and 26-30, which do not recite nucleic acid molecules "that encodes a maize or soybean phosphogluconate pathway enzyme or fragment thereof." As argued above, the specification describes nucleic acid molecules that hybridize under the recited conditions to, or comprise, the

claimed SEQ ID NOs. The Examiner has not presented any evidence to contradict this. Appellant has provided an adequate written description for the claimed invention. That is all that is required.

(4) Claims 2, 11-22, 25 and 27-30 are separately patentable

The Examiner argues that nucleic acid sequences that hybridize to the claimed nucleic acid molecules have not been described in the specification. Final Action at pages 8-9. The Examiner provides no support as to why one of skill in the art would not be able to recognize a nucleic acid molecule comprising a nucleic acid sequence that hybridizes to a sequence of SEQ ID NOs: 1, 4, 14, 27, 225, 298, 311, 356, 569 and 619 or complements or variations thereof under the recited conditions. The specification describes the claimed sequences and hybridization conditions. *See, e.g.*, specification at page 43, line 13 through page 45, line 4 and in the sequence listing. The skilled artisan would recognize that Appellant had possession of a nucleic acid sequence comprising the claimed SEQ ID NOs, as well as complements and variations thereof. Moreover, such a basis for rejection, even if valid, would not apply to claims 2, 11-22, 25 and 27-30, which do not recite to nucleic acid sequences that hybridizes under any recited conditions. The Examiner has not presented any evidence to contradict this. Appellant has provided an adequate written description for the claimed invention. That is all that is required.

(5) Claims 2, 22, 25 and 28 are separately patentable

The Examiner argues that "a genomic sequence significantly longer in length than a claimed fragment may still hybridize to a recited sequence under the claimed conditions are introns, etc. may 'bubble' out where mismatches occur." Final Action at page 7. The Examiner provides no support as to why one of skill in the art would not be able to recognize a nucleic acid molecule comprising a nucleic acid sequence that hybridizes to a recited SEQ ID NO or complements or variations thereof under the recited conditions.

The specification describes the claimed sequences and hybridization conditions. *See, e.g.*, specification at page 43, line 13 through page 45, line 4 and in the sequence listing. The skilled artisan would recognize that Appellant had possession of a nucleic acid sequence comprising the claimed SEQ ID NOs, as well as complements and variations thereof. Moreover, such a basis for rejection, even if valid, would not apply to claims 2, 22, 25 and 28, which do not recite nucleic acid sequence that encodes a phosphogluconate pathway enzyme or fragment thereof comprising a nucleic acid sequence that hybridizes under any recited conditions. The Examiner has not presented any evidence to contradict this. Appellant has provided an adequate written description for the claimed invention. That is all that is required.

(6) Claim 1, 2, 10-13, 15-22 and 24-30 are supported by a written description

In light of all of the arguments above, claims 1, 2, 10-13, 15-22 and 24-30 are supported by an adequate written description pursuant to the requirements of 35 U.S.C. § 112, and the rejection should be reversed.

CONCLUSION

In view of the foregoing, it is respectfully requested that the Board of Patent Appeals and Interferences reverse the Rejections and that the subject application be allowed forthwith.

Respectfully submitted,

Date: September 13, 2004

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APPENDIX A

1. A substantially purified nucleic acid molecule that encodes a maize or soybean phosphogluconate pathway enzyme or fragment thereof, wherein said maize or soybean phosphogluconate pathway enzyme is selected from the group consisting of:

(a) glucose-6-phosphate-1-dehydrogenase;

(b) D-ribulose-5-phosphate-3-epimerase; and

(c) phosphoglucoisomerase;

wherein said substantially purified nucleic acid molecule comprises a nucleic acid sequence that hybridizes under conditions of 6.0 X sodium chloride/sodium citrate (SSC) at about 45°C, followed by a wash of 2.0 X SSC at 50°C to a nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 1, 225, 619 and complements thereof.

2. The substantially purified nucleic acid molecule according to claim 1, wherein said substantially purified nucleic acid molecule comprises a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 1, 225, 619 and complements thereof.

10. An isolated nucleic acid molecule comprising a sequence that hybridizes under conditions of 6.0 X sodium chloride/sodium citrate (SSC) at about 45°C, followed by a wash of 2.0 X SSC at 50°C to a nucleic acid molecule comprising a nucleic acid

sequence selected from the group consisting of SEQ ID NOs: 1, 225, 619 and complements thereof.

11. An isolated nucleic acid molecule, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 1, 4, 14, 27, 225, 298, 311, 356, 569, and 619 or complements thereof.

12. The isolated nucleic acid molecule according to claim 11, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 1 or complement thereof.

13. The isolated nucleic acid molecule according to claim 11, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 4 or complement thereof.

15. The isolated nucleic acid molecule according to claim 11, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 27 or complement thereof.

16. The isolated nucleic acid molecule according to claim 11, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 225 or complement thereof.

17. The isolated nucleic acid molecule according to claim 11, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 298 or complement thereof.

18. The isolated nucleic acid molecule according to claim 11, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 311 or complement thereof.

19. The isolated nucleic acid molecule according to claim 11, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 356 or complement thereof.

20. The isolated nucleic acid molecule according to claim 11, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 569 or complement thereof.

21. The isolated nucleic acid molecule according to claim 11, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 619 or complement thereof.

22. A substantially purified nucleic acid molecule that encodes a maize or soybean 6-phosphogluconate dehydrogenase or fragment thereof, comprising a nucleic acid

sequence selected from the group consisting of SEQ ID NOs: 14, 27 and complements thereof.

24. A substantially purified nucleic acid molecule that encodes a maize or soybean phosphogluconate pathway enzyme or fragment thereof, wherein said maize or soybean phosphogluconate pathway enzyme is selected from the group consisting of:

(a) glucose-6-phosphate-1-dehydrogenase;

(b) D-ribulose-5-phosphate-3-epimerase;

(c) ribose-5-phosphate isomerase; and

(c) transaldolase;

wherein said substantially purified nucleic acid molecule comprises a nucleic acid sequence that hybridizes under conditions of 6.0 X sodium chloride/sodium citrate (SSC) at about 45°C, followed by a wash of 0.2 X SSC at 50°C to a nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 4, 298, 311, 569 and complements thereof.

25. The substantially purified nucleic acid molecule according to claim 24, wherein said substantially purified nucleic acid molecule comprises a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 4, 298, 311, 569 and complements thereof.

26. An isolated nucleic acid molecule comprising a sequence that hybridizes under conditions of 6.0 X sodium chloride/sodium citrate (SSC) at about 45°C, followed by a

wash of 0.2 X SSC at 50°C to a nucleic acid molecule comprising a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 4, 298, 311, 569 and complements thereof.

27. The isolated nucleic acid molecule according to claim 26, wherein said nucleic acid molecule comprises a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 4, 298, 311, 569 and complements thereof.

28. A substantially purified nucleic acid molecule that encodes a maize transketolase enzyme or fragment thereof comprising a nucleic acid sequence of SEQ ID NO: 356 or complement thereof.

29. The isolated nucleic acid molecule according to claim 10, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 1, 225, 619 and complements thereof.

30. The isolated nucleic acid molecule according to claim 11, wherein said isolated nucleic acid molecule comprises a nucleic acid sequence of SEQ ID NO: 14 or complement thereof.

31. An isolated nucleic acid molecule, wherein said nucleic acid molecule consists of a nucleic acid sequence selected from the group consisting of SEQ ID NOs: 1, 4, 14, 27, 225, 298, 311, 356, 569, and 619 or complements thereof.

APPENDIX B

Paper No. 17

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte DANE K. FISHER, and RAGHUNATH V. LALGUDI

Appeal No. 2002-2046
Application No. 09/619,643

HEARD: March 16, 2004

Before WILLIAM F. SMITH, ADAMS, and GRIMES, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claim 1, the only claim pending in the application, reproduced below:

1. A substantially purified nucleic acid molecule that encodes a maize protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO:5.

The examiner does not rely on a reference.

GROUNDS OF REJECTION

Claim 1 stands rejected under 35 U.S.C. § 101 as lacking utility and § 112, first paragraph, for lack of enablement based on the finding of lack of utility. Claim 1 also stands rejected under 35 U.S.C. § 112, first paragraph, as the specification fails to provide an adequate written description of the claimed invention. We affirm the utility and enablement rejections. We reverse the written description rejection.

BACKGROUND

The subject matter of the present appeal is directed to expressed sequence tags (ESTs). See Specification, page 15, lines 9-10. ESTs "are short sequences of randomly selected clones from a cDNA (or complementary DNA) library which are representative of the cDNA inserts of these randomly selected clones." Specification, page 1.

As set forth at page 9, lines 2-4, of appellants' specification "[t]he present invention provides a substantially purified nucleic acid molecule that encodes a maize protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 32236." Of these 32,236 nucleic acid sequences, the originally filed claims where directed to SEQ ID NO: 1 through SEQ ID NO: 4,013. On January 26, 2001 (Paper No. 4), the examiner entered a Restriction requirement into the record, requiring, inter alia, appellants "to elect up to 5 nucleic acid sequences" for consideration on the merits. Paper No. 4, page 3. In response, appellants elected SEQ ID NO:1 through SEQ ID NO:5. The ESTs set forth in SEQ ID NO: 1 through SEQ ID NO:

5 are disclosed to be obtained from cDNA library LIB3115 "generated from maize (RX601, Asgrow Seed Company, Des Moines, Iowa U.S.A.) pooled leaf tissue...." Specification, pages 79-80, Example 1.

The specification sets forth a number of utilities for the nucleic acid molecules of SEQ ID NO: 1 through SEQ ID NO: 5 which are summarized by the examiner (Answer, bridging paragraph, pages 5-6) as follows:

> The specification teaches that the nucleic acids may be used to produce a plant containing reduced levels of a protein (pg. 11), determining an association between a polymorphism and a plant trait (pg. 11), isolating a genetic region or nucleic acid (pg. 11), determining a level or pattern in a plant cell of a protein in a plant (pg. 11), determining a mutation in a plant whose presence is predictive of a mutation affecting a level or pattern of a protein (pg. 13), as molecular tags to isolate genetic regions, isolate genes, map genes, and determine gene function (pg. 14), and identifying tissues (pg. 14)[.] The specification states that the nucleic acid ESTs of the present invention can enable the acquisition of molecular markers, which can be used in breeding schemes, genetic and molecular mapping and cloning of agronomically significant genes (pg. 31).

In the examiner's opinion "[t]hese are non-specific uses that are applicable to nucleic acids in general and not particular or specific to the nucleic acids being claimed." Answer, page 6. For example, the examiner finds (Answer, page 10), "determining whether the claimed nucleic acids have or do not have a polymorphism would require determining whether there was a polymorphism within such a sequence and then determining how to use this information in a patentably meaningful way."[1]

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[1] During the Oral Hearing, appellants' representative confirmed that the administrative file contained no evidence that the claimed ESTs where capable of detecting a polymorphism that correlated with any particular trait.

In presenting their case on appeal, appellants focus on use of the claimed nucleic acid molecules to identify the presence or absence of a polymorphism, and their use as probes or as a source for primers. See e.g., Brief, pages 6-12. According to appellants (Brief, page 3), "they have disclosed nucleic acid molecules which, in their current form, provide at least one specific benefit to the public, for example the ability to identify the presence or absence of a polymorphism in a population of maize plants." Furthermore, appellants assert (Brief, page 8), "[t]he specification discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms...."

CLAIM CONSTRUCTION

As set forth above, claim 1 on appeal is drawn to a substantially purified nucleic acid molecule that encodes a maize protein or fragment thereof comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO:5. According to appellants' specification (page 15, lines 19-25), the term "substantially purified"

> refers to a molecule separated from substantially all other molecules normally associated with it in its native state. More preferably a substantially purified molecule is the predominant species present in a preparation. A substantially purified molecule may be greater than 60% free, preferably 75% free, more preferably 90% free, and most preferably 95% free from the other molecules (exclusive of solvent) present in the natural mixture. The term "substantially purified" is not intended to encompass molecules present in their native state.

As we understand the claimed invention the use of the transitional term "comprising" does not allow for internal alterations (e.g. insertions or deletions) of

the nucleotide sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 5, but instead only allows for the addition of nucleotides or other molecules at either end of the nucleotide sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 5.[2] In this regard, we recognize, as does the examiner (Answer, page 14), the claim as written encompasses, inter alia, genes, full open reading frames, fusion constructs, and cDNAs.

Accordingly, for the purposes of our review, we interpret the claimed invention as drawn to a nucleic acid molecule, separated from substantially all other molecules normally associated with it in its native state, selected from the group consisting of the nucleic acid molecule defined by the 429 nucleotide sequence set forth in SEQ ID NO: 1, the 413 nucleotide sequence set forth in SEQ ID NO: 2, the 365 nucleotide sequence set forth in SEQ ID NO: 3, the 414 nucleotide sequence set forth in SEQ ID NO: 4, and the 333 nucleotide sequence set forth in SEQ ID NO: 5, with or without any preceding or trailing nucleotides, or other molecules.

DISCUSSION

Utility

The starting point for determining whether a nucleic acid molecule selected from the group consisting of SEQ ID NO: 1 through SEQ ID NO: 5

[2] This interpretation of the claimed invention was confirmed by appellants' representative during the Oral Hearing.

possesses utility under 35 U.S.C. § 101 is Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966). As set forth in Brenner, at 534-35, 148 USPQ at 695[3],

> the basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until [an invention] is refined and developed to this point--where specific benefit exists in currently available form--there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.

In considering the issues presented in this appeal, special attention must be paid to the Brenner court's statement that a patent should issue only when an invention possesses "substantial utility," i.e., "where a specific benefit exists in currently available form." Whether a claimed invention is useful under 35 U.S.C. § 101 is a question of fact. Cross v. Iizuka, 753 F.2d 1040, 1044 n.7, 224 USPQ 739, 742 n.7 (Fed. Cir. 1985).

At issue in Brenner was a claim to "a chemical process which yields an already known product whose utility—other than as a possible object of scientific inquiry—ha[d] not yet been evidenced." Id. at 529, 148 USPQ at 693. The Patent Office had rejected the claimed process for lack of utility, on the basis that the product produced by the claimed process had not been shown to be useful. See id. at 521-22, 148 USPQ at 690. On appeal, the Court of Customs and Patent Appeals reversed, on the basis that "where a claimed process produces a

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[3] In discussing the issue of utility under 35 U.S.C. § 101, the Federal Circuit and the Court of Customs and Patent Appeals since Brenner, have used the phrases "substantial utility" and "practical utility" interchangeably. See e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1963-1964, 39 USPQ2d 1895, 1898-1899 (Fed. Cir. 1996) ("It is well established that a patent may not be granted to an invention unless substantial or practical utility for the invention has been discovered and disclosed.").

known product it is not necessary to show utility for the product." Id. at 522, 148 USPQ at 691.

The Brenner Court noted that although § 101 requires that an invention be "useful," that "simple, everyday word can be pregnant with ambiguity when applied to the facts of life." Id. at 529, 148 USPQ at 693. Thus,

> [i]t is not remarkable that differences arise as to how the test of usefulness is to be applied to chemical processes. Even if we knew precisely what Congress meant in 1790 when it devised the "new and useful" phraseology and in subsequent re-enactments of the test, we should have difficulty in applying it in the context of contemporary chemistry, where research is as comprehensive as man's grasp and where little or nothing is wholly beyond the pale of "utility"—if that word is given its broadest reach.

Id. at 530, 148 USPQ at 694.[4]

The Court, finding "no specific assistance in the legislative materials underlying § 101," based its analysis on "the general intent of Congress, the purposes of the patent system, and the implications of a decision one way or the other." Id. at 532, 148 USPQ at 695. The Court concluded that "[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." Id. at 534-35, 148 USPQ at 695.

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[4] The invention at issue in Brenner was a process, but the Court expressly noted that its holding "would apply equally to the patenting of the product produced by the process." Id. at 535, 148 USPQ at 695-96.

The Court considered and rejected the applicant's argument that attenuating the requirement of utility "would encourage inventors of new processes to publicize the event for the benefit of the entire scientific community, thus widening the search for uses and increasing the fund of scientific knowledge." The Court noted that, while there is value to encouraging disclosure, "a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development." Id. at 534, 148 USPQ at 695.

The Court took pains to note that it did not "mean to disparage the importance of contributions to the fund of scientific information short of the invention of something 'useful,'" and that it was not "blind to the prospect that what now seems without 'use' may tomorrow command the grateful attention of the public." Id. at 535-36, 148 USPQ at 696. Those considerations did not sway the Court, however, because "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." Id.

Subsequent decisions of the CCPA and the Court of Appeals for the Federal Circuit have added further layers of judicial gloss to the meaning of

§ 101's utility requirement. The first opinion of the CCPA applying Brenner was In re Kirk, 376 F.2d 936, 153 USPQ 48 (CCPA 1967). The invention claimed in Kirk was a set of steroid derivatives said to have valuable biological properties and to be of value "in the furtherance of steroidal research and in the application of steroidal materials to veterinary or medical practice." Id. at 938, 153 USPQ at 50. The claims had been rejected for lack of utility. In response, the applicants submitted an affidavit which purportedly "show[ed] that one skilled in the art would be able to determine the biological uses of the claimed compounds by routine tests." Id. at 939, 153 USPQ at 51.

The court held that "nebulous expressions [like] 'biological activity' or 'biological properties'" did not adequately convey how to use the claimed compounds. Id. at 941, 153 USPQ at 52. Nor did the applicants' affidavit help their case: "the sum and substance of the affidavit appear[ed] to be that one of ordinary skill in the art would know 'how to use' the compounds to find out in the first instance whether the compounds are—or are not—in fact useful or possess useful properties, and to ascertain what those properties are." Id. at 942, 153 USPQ at 53.

The Kirk court held that an earlier CCPA decision, holding that a chemical compound meets the requirements of § 101 if it is useful to chemists doing research on steroids, had effectively been overruled by Brenner. "There can be no doubt that the insubstantial, superficial nature of vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the

researcher' was recognized, and clearly rejected, by the Supreme Court" in Brenner. See Kirk, 376 F.2d at 945, 153 USPQ at 55.

More recently, in In re Ziegler, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993), the Federal Circuit considered the degree of specificity required to show utility for a claim to polypropylene. The U.S. application on appeal in Ziegler claimed priority to a German application filed in 1954. "In the German application, Ziegler disclosed only that solid granules of polypropylene could be pressed into a flexible film with a characteristic infrared spectrum and that the polypropylene was 'plastic-like.'" Id. at 1203, 26 USPQ2d at 1605. "Ziegler did not assert any practical use for the polypropylene or its film, and Ziegler did not disclose any characteristics of the polypropylene or its film that demonstrated its utility." Id. The court held that the German application did not satisfy the requirements of § 101 and therefore could not be relied on to overcome a rejection based on an intervening reference. Id. "[At] best, Ziegler was on the way to discovering a practical utility for polypropylene at the time of the filing of the German application; but in that application Ziegler had not yet gotten there." Id.

On the other hand, the CCPA reversed a rejection for lack of utility in In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980). The applicant in Jolles claimed pharmaceutical compositions that were disclosed to be useful in treating acute myeloblastic leukemia. See id. at 1323, 206 USPQ at 886. The active ingredients in the compositions were closely related to daunorubicin and doxorubicin, both of which were "well recognized in the art as valuable for use in

cancer chemotherapy." Id., 206 USPQ at 887. The applicant also submitted declaratory evidence showing that eight of the claimed compositions were effective in treating tumors in a mouse model, and one was effective in treating humans. See id. at 1323-24, 206 USPQ at 887-88. The court noted that the data derived from the mouse model were "relevant to the treatment of humans and [were] not to be disregarded," id. at 1327, 206 USPQ at 890, and held that the evidence was sufficient to support the asserted therapeutic utility. See id. at 1327-28, 206 USPQ at 891.

The Federal Circuit held in Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), that in vivo testing (as in Jolles) was not necessarily required to show utility in the pharmaceutical context. The Cross court stated that "[it] is axiomatic that an invention cannot be considered 'useful,' in the sense that a patent can be granted on it, unless substantial or practical utility for the invention has been discovered and disclosed where such utility would not be obvious." Id. at 1044, 224 USPQ at 742 (citing Brenner v. Manson). The court "perceive[d] no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for the compound in question." Id. at 1051, 224 USPQ at 748. Successful in vitro testing could provide an immediate benefit to the public, by "marshal[ling] resources and direct[ing] the expenditure of effort to further in vivo testing of the most potent compounds ..., analogous to the benefit provided by the showing of an in vivo utility." Id. On the facts of that case – successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar

compounds – the court held that in vitro activity was sufficient to meet the requirements of § 101. See id.

The Federal Circuit confirmed in In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995), that human testing is not necessary to establish utility for a method of treatment. The invention claimed in Brana was a group of compounds disclosed to have antitumor activity. See id. at 1562, 34 USPQ2d at 1437-38. The specification disclosed that the claimed compounds had higher antitumor activity than related compounds known to have antitumor activity, and the applicants provided declaratory evidence of in vivo activity against tumors in a mouse model. See id., 34 USPQ2d at 1438. The court held that these data were sufficient to satisfy § 101; usefulness in patent law does not require that the invention be ready to be administered to humans. See id. at 1567, 34 USPQ2d at 1442.

Several lessons can be drawn from Brenner and its progeny. First, § 101's requirement that an invention be "useful" is not to be given its broadest reach, such that little or nothing of a chemical nature would be found to lack utility. See Brenner, 383 U.S. at 530, 148 USPQ at 694. Thus, not every "use" that can be asserted will be sufficient to satisfy § 101. For example, the steroid compound at issue in Brenner was useful as a possible object of scientific inquiry, and the polypropylene claimed in Ziegler was useful for pressing into a flexible film, yet both lacked sufficient utility to satisfy § 101. See Brenner, 383 U.S. at 529, 148 USPQ at 696; Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

Rather than setting a de minimis standard, § 101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form. Brenner, 383 U.S. at 534-35, 148 USPQ at 695. This standard has been found to be met by pharmaceutical compositions shown to be useful in mouse models and in humans for treating acute myeloblastic leukemia (Jolles, 628 F.2d at 1327-28, 206 USPQ at 891); by evidence showing successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds (Cross, 753 F.2d at 1051, 224 USPQ at 748); and by evidence showing in vivo antitumor activity in mice, combined with a disclosure that the claimed compounds had higher antitumor activity than a related compound known to have antitumor activity (Brana, 51 F.3d at 1567, 34 USPQ2d at 1442).

By contrast, Brenner's standard has been interpreted to mean that "vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher'" would not satisfy § 101. See Kirk, 376 F.2d at 945, 153 USPQ at 55 (interpreting Brenner). Likewise, a disclosure of a "plastic-like" polypropylene capable of being pressed into a flexible film was held to show that the applicant was "at best ... on the way to discovering a practical utility for polypropylene at the time of the filing," but not yet there. Ziegler, at 1203, 26 USPQ2d at 1605.

With these principles in mind we turn to the issues at hand. Of the many utilities asserted in the specification, two have received the most attention in the briefing in this appeal, i.e., identification and detection of polymorphisms and use

as probes or as a source for primers. We shall focus on these asserted utilities first and then address the other arguments set forth in the briefing.

a. Polymorphisms

This utility is discussed at pages 35-42 of the specification in terms of what polymorphisms are and how one would go about determining the existence of a polymorphism. The discussion in this portion of the specification, however, is not specific to the nucleotide molecules depicted in SEQ ID NO: 1 through SEQ ID NO: 5. To the contrary, according to appellants' specification (page 35, lines 25-26), "one or more of the [32,236] EST nucleic acid molecules (or a sub-fragment thereof) may be employed as a marker nucleic acid molecule to identify ... polymorphism(s)." The specification does not explain why any of the 32,236 nucleotide molecules disclosed in the specification, or more specifically the five nucleotide molecules depicted in SEQ ID NO: 1 through SEQ ID NO: 5, would in fact be useful in detecting polymorphisms.

Rather, appellants argue (Brief, page 7), "the claimed nucleic acid molecules have utility even if the absence of a particular polymorphism is detected. Indeed, the absence of a polymorphism usually demonstrates that the two (or more) populations being compared share a common genetic heritage." In other words, appellants' position is that an EST by definition possesses patentable utility because it can be used by itself in determining whether populations share a common genetic heritage. While that may be a "utility," we do not find that it is a substantial utility.

Without knowing any further information in regard to the gene represented by an EST, as here, detection of the presence or absence of a polymorphism provides the barest information in regard to genetic heritage. As the examiner explains (Answer, bridging paragraph, pages 10-11):

> Polymorphisms are natural variations within sequences which themselves may not have any meaningful use. Therefore, determining whether the claimed nucleic acids [(or nucleic acids detected by the claimed nucleic acids)] have or do not have a polymorphism would require determining whether there was a polymorphism within such a sequence and then determining how to use this information in a patentably meaningful way. The [a]ppellant also argues, "many of these uses are directly analogous to a microscope". This argument has been reviewed but is not convincing because the microscope provides information to the scientist which is automatically useful. For example, the microscope may be used for identification and differentiation between gram-positive and gram-negative bacteria. The differentiation of bacteria facilitates in the administration of proper antibiotics. For example, if the microscope is used to determine whether Staph is present or whether Strep is present provides valuable information to the scientist and/or doctor for treating patients. The instant invention, however, provides no information to this extent. If the scientist determines that SEQ ID NO: 1 is present, the scientist does not know how to use this information. Thus, the identification of SEQ ID NO: 1 is not a substantial utility.

In contrast, at the other end of the "utility spectrum" would be information gleaned from detecting the presence or absence of a polymorphism when it is known what effect the gene from which the EST is derived has in the development and/or phenotype of the plant. Somewhere between having no knowledge (the present circumstances) and having complete knowledge of the gene and its role in the plant's development and/or phenotype lies the line between "utility" and "substantial utility." We need not draw the line or further

define it in this case because the facts in this case represent the lowest end of the spectrum, i.e., an insubstantial use.

b. Probes or source of primers

Appellants argue that the "specification discloses that the claimed nucleic acid molecules can be used to isolate nucleic acid molecules of other plants and organisms...." Appeal Brief, page 8. While that may be true, it begs the question of what substantial use such nucleic acid molecules would have? Again, the present specification does not attribute any property in terms of plant trait, or phenotype to any of the nucleotide molecules set forth in SEQ ID NO: 1 through SEQ ID NO: 5. In the absence of such information, using the claimed molecules to isolate other molecules, which themselves lack substantial utility, does not represent a substantial utility.

Appellants also assert that the claimed nucleic acid molecules may be used in a "chromosome walk." Brief, pages 8-9. According to appellants (Brief, page 9),

> The claimed nucleic acid molecules provide a particularly appropriate and demonstrably useful starting point for a walk to isolate a promoter that is active in leaves at the time of anthesis. Isolation of such a promoter would be desirable and particularly useful because it allows expression of proteins at that important developmental state, including proteins that provide disease resistance. Because the claimed nucleic acid molecules were isolated from leaves, they provide an appropriate starting point for isolating a promoter active in leaves. A random nucleic acid molecule does not provide an equally good starting point to isolate such a promoter.

As we understand this argument, the claimed ESTs may be useful in searching for promoters that are only active in leaves at the time of anthesis. The

specification, however, fails to demonstrate that any of the nucleic acid molecules set forth in SEQ ID NO: 1 through SEQ ID NO: 5 would be useful in obtaining a successful result from such a search. As set forth at page 34, lines 14-19 of appellants' specification,

> The [32,236] nucleic acid molecules of the present invention may be used to isolate promoters of tissue enhanced[,] tissue specific, cell-specific, cell –type, developmentally or environmentally regulated expression profiles. Isolation and functional analysis of the 5' flanking promoter sequences of these genes from genomic libraries, for example, using genomic screening methods and PCR techniques would result in the isolation of useful promoters and transcriptional regulatory elements.

The specification does not provide any expectation of successfully using any of the 32,236 nucleic acid molecules disclosed in the specification, or more specifically the five nucleic acid molecules depicted in SEQ ID NO: 1 through SEQ ID NO: 5, to isolate promoters of tissue enhanced, tissue specific, cell-specific, cell–type, developmentally or environmentally regulated expression profiles.

Furthermore, notwithstanding appellants' assertion (Brief, page 9), there is no evidence on this record that any of the nucleic acid molecules depicted in SEQ ID NO: 1 through SEQ ID NO: 5 are tissue or cell-type specific, or developmentally or environmentally regulated. In this regard, we note that the claimed nucleic acid molecules were isolated from the cDNA library LIB3115. Specification, page 80, lines 5-6. There is no evidence on this record that LIB3115 is a subtractive cDNA library, wherein nucleic acid molecules from other maize tissue, or from other developmental stages, was subtracted (removed)

from the library. Compare, for example, the subtractive cDNA library LIB3153 which is disclosed (specification, page 83, lines 17-19) to be "generated by subtracting driver cDNA, which is prepared from kernels harvested from 15 DAP [days after pollination] maize plants, from target cDNA, which is prepared from endosperms harvested from 5-8 day[s] after pollination (DAP) maize plants." In contrast to the claimed nucleic acid molecules, nucleic acid molecules SEQ ID NO: 24,931 through SEQ ID NO: 25,680 are from the subtractive cDNA library LIB3153.

In our opinion, the claimed nucleic acid molecules having the sequences identified as SEQ ID NO: 1 through SEQ ID NO: 5, represent five randomly selected nucleic acid molecules isolated from pooled leaf tissue at the time of anthesis. Notwithstanding appellants' emphasis on "anthesis," for the foregoing reasons, we find no evidence on this record that any of appellants' five randomly selected nucleic acid molecules are expressed only at the time of "anthesis." Accordingly, despite appellants' assertion to the contrary, there is no reasonable expectation that any of the claimed nucleic acid molecules would be capable of isolating a promoter that was only active in leaves at the time of anthesis. As appellants recognize (Brief, page 9), "[a] random nucleic acid molecule does not provide an equally good starting point to isolate such a promoter" compared to a nucleic acid molecule that is known to be specifically associated with this stage of plant development.

We recognize appellants' argument (Brief, bridging sentence, pages 9-10), "[a]n invention may be 'less effective than existing devices but nevertheless

meet the statutory criteria for patentability.' Custom Accessories, Inc. v. Jeffrey-Allan Indus., 807 F.2d 955, 960 n.12, 1 U.S.P.Q.2d 1196, 1199 n.12 (Fed. Cir. 1986)." While we agree with appellants' statement, we fail to see how it applies to appellants' claimed invention, wherein there is no evidence or expectation that the claimed nucleic acid molecules would be "effective" at all. In this regard, we remind appellants that an invention does not have utility sufficient to satisfy § 101 until it is "refined and developed" to the point of providing a specific benefit in currently available form. See, e.g., Brenner, 383 U.S. at 534, 148 USPQ at 695.

An invention certainly can have a utility that is shared by other compounds or compositions. Take, for example, an application that claims ibuprofen and discloses that it is useful as an analgesic. No one would argue that a claim to ibuprofen lacks utility simply because aspirin and acetaminophen are also useful as analgesics. On the other hand, not every utility will satisfy § 101, even if the utility is shared by a class of inventions. Assume that the above-described application did not disclose that ibuprofen was an analgesic but only disclosed that it is useful because it can be used to fill a jar, which would then be useful as a paperweight. There would be little doubt that this disclosed utility would not satisfy § 101, even though the utility is shared by a large class of inventions, viz., those whose physical embodiments have mass. So while a utility need not be unique to a claimed invention, it must nonetheless be specific, and in currently available form, in order to satisfy § 101.

c. Other Arguments

Appellants argue that the specification "discloses additional utilities for the claimed nucleic acid molecules including introduction of the claimed nucleic acid molecules into a plant or plant cell (either as sense or antisense inhibitors), which can then be used to screen for compounds such as a herbicide." Brief, page 6. Specifically, appellants argue (id.) that "a compound can be provided to both an antisense plant and a control plant (no antisense) and the effect of the compound on the plant can be monitored." Appellants analogize this proposed procedure to a "cell-based assay" which appellants assert to have a "legally sufficient utility." Id.

Suffice it to say that an otherwise uncharacterized nucleic acid molecule is being claimed in this application, not an assay. The portion of the specification cited in support of this argument (page 73, line 17 through page 74, line 17) indicates that the nucleic acid molecule must be introduced into a plant cell and transcribed using an appropriate promoter to result in the suppression of an endogenous protein. The specification does not indicate that such a method is feasible when the nucleic acid to be used is uncharacterized[5] as here. Such a use does not provide a specific or substantial benefit in currently available form.

Appellants also argue that the claimed nucleic acids are useful to measure the level of mRNA in a sample through use of microarray technology

[5] To emphasize the uncharacterized nature of appellants' invention we note the examiner's finding (Answer, page 17) that translating SEQ ID NO: 5 in all 6 possible reading frames reveals that the sequence contains numerous stop codons which would terminate the translation of a protein, or protein fragment, encoded thereby.

and use as molecular markers. Brief, page 6. In regard to microarrays, appellants argue (id. fn. 3) that it is "standard practice" to screen populations of nucleic acids with EST sequences without characterizing each and every target mRNA. We find that the asserted utility of the claimed nucleic acid—as one component of an assay for monitoring gene expression—does not satisfy the utility requirement of § 101. Such a use does not provide a specific benefit in currently available form. We accept, for argument's sake, that a person skilled in the art could use the claimed nucleic acid, in combination with other nucleic acids, to monitor changes in expression of the gene that encompasses the nucleic acid depicted in e.g., SEQ ID NO: 1. However, the specification provides no guidance that would allow a skilled artisan to use data relating to expression of such a gene in any practical way. The specification simply provides no guidance regarding what the SEQ ID NO: 1-specific information derived from a gene expression experiment would mean. As the examiner points out (Answer, page 9), "the instant claimed nucleic acids appear to require further experimentation on the material itself to determine the function and properties of the claimed nucleic acids."

To highlight the examiner's assertion, suppose, for example, that a researcher found that SEQ ID NO: 1 expression was increased when a cell was treated with a particular agent. The specification provides no basis on which a skilled worker would be able to determine whether that result is meaningful. Maybe the meaning in a change in SEQ ID NO: 1 expression would depend on other factors, but again the specification provides no hint as to what other factors

might be important. Would it depend on what agent is used, what cell type is used, the behavior of other genes (if so, which genes and what behavior is significant), the degree of increase? The specification simply provides no guidance as to how to interpret the results that might be seen using SEQ ID NO: 1 in a gene expression assay.

In effect, appellants' position is that the claimed nucleic acids are useful because those of skill in the art could experiment with them and figure out for themselves what any observed experimental results might mean. We do not agree that such a disclosure provides a "specific benefit in currently available form." Rather, the present case seems analogous to Brenner. In Brenner, the applicant claimed a method of making a compound but disclosed no utility for the compound. 383 U.S. at 529, 148 USPQ at 693. The Court held that a process lacks utility if it produces a product that lacks utility. Id. at 534, 148 USPQ at 695. Here, appellants claim a product asserted to be useful in a method of generating gene-expression data, but the specification does not disclose how to interpret those data. Just as the process claimed in Brenner lacked utility because the specification did not disclose how to use the end-product, the products claimed here lack utility, because even if used in gene expression assays, the specification does not disclose how to use SEQ ID NO: 1-specific gene expression data.

Assuming arguendo, that a generic gene expression assay—one based on monitoring expression of thousands of uncharacterized nucleic acids would provide a useful tool for, e.g., drug discovery, it does not follow that each one of

the nucleic acids represented in the assay individually has patentable utility. Although each nucleic acid in the assay contributes to the data generated by the assay overall, the contribution of a single nucleic acid—its data point—is only a tiny contribution to the overall picture. The Brenner Court held that § 101 sets more than a de minimis standard for utility. Therefore, the patentable utility of a gene expression assay, for example, does not necessarily mean that each tiny component of the assay also has patentable utility. A patentable utility divided by a thousand does not necessarily equal a thousand patentable utilities. Each claimed invention must be shown to meet § 101's utility requirement in order to be patentable; it must provide a specific benefit in currently available form. Providing a single data point among thousands or millions, even if the thousands or millions of data points collectively are useful, does not meet this standard. The Supreme Court noted that the patent system contemplates a basic quid pro quo: in exchange for the legal right to exclude others from his invention for a period of time, an inventor discloses his invention to the public. See Brenner, 383 U.S. at 534, 148 USPQ at 695. The Brenner Court held that the grant of patent rights to an applicant is justified only by disclosure of an invention with substantial utility – a specific benefit in currently available form. Until the invention has been refined and developed to this point, the Court held, the applicant has not met his side of the bargain, and has not provided a disclosure sufficient to justify a grant of the right to exclude others. See id.

We reach the same conclusion in regard to appellants' assertion that the nucleic acid molecules depicted in SEQ ID NO: 1 through SEQ ID NO: 5 are

useful as a molecular marker or probe. It is not seen that the one data point which may be provided by using the uncharacterized nucleic acid molecule of SEQ ID NO: 1 as a molecular marker or probe represents a substantial use.

Appellants argue that ESTs have real world value as seen from the "growth of a multi-million dollar industry in the United States premised on the usefulness of ESTs." Brief, page 11. Since appellants fail to provide any suggestion on which use of ESTs this industry is premised on, we can only assume that appellants are referring to the potential usefulness of EST databases, clone sets or microarrays. Suffice it to say, the claims on appeal are not directed to EST databases, clone sets and/or microarrays. Again, it is not seen that the one data point which may be provided by using the uncharacterized nucleic acid molecules of SEQ ID NO: 1 through SEQ ID NO: 5 in such devices represents a substantial use.

For the foregoing reasons we affirm the rejection of claim 1 under 35 U.S.C. § 101.

Enablement

According to the examiner (Answer, page 13, emphasis removed), "since the claimed invention is not supported by either a specific, substantial asserted utility or a well established utility for the reasons set forth [in support of the rejection under 35 U.S.C. § 101] one skilled in the art clearly would not know how to use the claimed invention." This rejection is simply a corollary of the finding of lack of utility. Appellants assert (Brief, page 12), this rejection should be reversed for the same reasons set forth in their arguments regarding the

rejection under 35 U.S.C. § 101. Thus, our conclusion with respect to the § 101 issue will also apply to this aspect of the § 112 (enablement) issue. On this basis we affirm the rejection of claim 1 under the enablement provision of 35 U.S.C. § 112, first paragraph.

Written description

This rejection stands on a different footing. As we understand the examiner's argument the use of the transitional phrase "comprising" in appellants' claimed invention results in appellants claiming a large genus of nucleic acid molecules which are not adequately described by SEQ ID NO: 1 through SEQ ID NO: 5. Answer, pages 13-16. Apparently the examiner is of the opinion that the claimed invention should be limited to nucleic acid molecules as set forth in SEQ ID NO: 1 through SEQ ID NO: 5. In response appellants argue (Brief, page 14, original footnote omitted),

> Applicants have provided the nucleotide sequences required by the claims, i.e., SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, and SEQ ID NO: 5, and have thus established possession of the claimed invention. The fact that the claims at issue are intended to cover molecules that include the recited sequences joined with additional sequences[6] does not mean that [a]pplicants were any less in possession of the claimed nucleic acid molecules.

As discussed supra, as we understand the claimed invention, the use of the transitional term "comprising" does not allow for internal alterations (e.g. insertions or deletions) of the nucleotide sequences set forth in SEQ ID NO: 1

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[6] By way of examples appellants explain (Brief, bridging paragraph, pages 14-15) that the specification discloses, inter alia, the claimed nucleic acid molecules joined together with vectors, and other nucleic acids (e.g. fusion nucleic acid molecules) and detectable labels.

through SEQ ID NO: 5, but instead only allows for the addition of nucleotides or other molecules at either end of the nucleotide sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 5. We agree with appellants that they have provided an adequate written description of nucleic acid molecules with the sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 5. That the claimed nucleic acid molecules may have other molecules attached to either, or both of their 5' or 3' ends does not diminish appellants' adequate written description of the nucleic acids molecules with the sequences set forth in SEQ ID NO: 1 through SEQ ID NO: 5 as claimed.

Accordingly, we reverse the rejection of claim 1 under the written description provision of 35 U.S.C. § 112, first paragraph.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

William F. Smith
Administrative Patent Judge

Donald E. Adams
Administrative Patent Judge

Eric Grimes
Administrative Patent Judge

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Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Re: U.S. Patent Application No. 09/300,482
Filed: April 28, 1999
Inventors: Nordine CHEIKH *et al.*
Title: **Nucleic Acid Molecules and Other Molecules Associated with the Phosphogluconate Pathway**
Atty. Dkt: 16517.216

Sir:

The following documents are transmitted herewith for appropriate action by the U.S. Patent and Trademark Office (PTO):

1. Appellant's Brief with attached Appendix A and Appendix B; and
2. a return postcard.

Please stamp the attached postcard with the filing date of these documents and return it to our courier.

Authorization is hereby given to charge the statutory fee of $330.00 for filing Appellant's Brief to Arnold & Porter LLP Deposit Account No. 50-2387, referencing docket number 16517.216. A duplicate copy of this letter is enclosed.

In the event that extensions of time are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned. Applicants do not believe any additional fees are due in conjunction with this filing. However, if any fees are required in the present application, including any fees for extensions of time, then the Commissioner is hereby authorized to charge such fees to Arnold & Porter LLP Deposit Account No. 50-2387, referencing docket number 16517.216.

Respectfully submitted,

David R. Marsh (Reg. No. 41,408)
Thomas E. Holsten (Reg. No. 46,098)

Attachments